Abstract

Transcription and pre-mRNA processing, e.g., splicing, occur at the same place and time in the context of chromatin. A growing amount of evidence supports the hypothesis that these processes are interconnected. Prp45/SKIP is one of the factors which are believed to mediate the interconnection. The human ortholog, SKIP, is known for affecting mRNA formation on the levels of transcription initiation and elongation. Moreover, it interacts with chromatin modifiers and it is a splicing factor, too. The function of the *Saccharomyces cerevisiae* ortholog, Prp45, has been so far connected only to pre-mRNA splicing.

In this work, we characterized the role of Prp45 in splicing and elaborated the results connecting Prp45 to transcription and chromatin modifications. RNA-seq results showed that pre-mRNA is accumulated in *prp45*(1-169) cells. This accumulation is not caused by the reduced activity of pathways responsible for RNA degradation. The extent of the splicing inefficiency in *prp45*(1-169) cells did not depend on either the canonicity of the 5' splice site and branch site or the distance between the branch site and the 3' splice site. Using chromatin immunoprecipitation, we found that *prp45*(1-169) mutation causes delay in U2 snRNP recruitment to assembling spliceosome. This delay transfers to the later phases of spliceosome assembly rendering the cotranscriptional recruitment of U5 snRNP and NTC complex almost undetectable. mRNA levels in the mutant cells are only marginally affected. Therefore, we suppose shift towards the posttranscriptional splicing, which makes splicing reaction less efficient.

We have observed that *prp45*(1-169) delays transcriptional induction of intronless genes, e.g., genes of phosphate metabolism. Based on Synthetic genetic array (SGA) results, *PRP45* genetically interacts with many genes encoding proteins involved in transcription elongation and chromatin modifications. The strongest interactions were found with genes coding histone variant H2A.Z and SWR1 complex components which load H2A.Z to chromatin. We analyzed the functional relationship between Prp45 and H2A.Z with the help of novel mutant alleles, *prp45*(1-247) and *prp45*(1-330).

Hypotheses are discussed about the function of Prp45 in interconnection of splicing, chromatin modifications and transcription.